REMARKS

Claims 1, 6, 19 and 21 have been amended to correct minor informalities and dependencies. Claims 1 and 6 have been amended to remove any reference to truncated polypeptides, however, Applicants reserve the right to pursue these variants in later filed applications. Claims 40-45 have been added. Support for new Claims 40-45 can be found in the Specification and Claims as filed, for example, Claims 1-4, 6 and 17. The changes made to the Claims by the current amendment, including ~~deletions~~ and additions, are shown herein with deletions designated with a strikethrough and additions underlined. No new matter has been added herewith. Upon allowance of the claims, Applicants request rejoinder of Claims 21 and 39 as being dependent upon an allowed claim. As a result of the amendments herein, Claims 1-4, 6-8, 10-11, 13-14, 17-21, and 39-45 are presented for further examination.

FlgE

Applicants would like the Examiner to note that the polypeptide is referred to as FlgE not "FigE" and that it refers to a polypeptide of a flagellar hook protein (see the Brief Description of the Drawings Figure 1).

Priority date

The Examiner erroneously stated the priority date as 5/11/2001 to the PCT application PCT/AU00/000437. However, to clarify the record, as shown in the Preliminary Amendment filed with the application, the priority date is to U.S. Provisional application 60/133973, filed May 13, 1999.

Claim Objection

The Examiner objected to Claim 19 as depending from cancelled claim 16. However, Claim 19 has been amended to depend from Claim 17, rendering the rejection moot.

Rejection Under 35 U.S.C.§112, first paragraph (Written Description)

The Examiner has rejected Claims 1-4, 6-8, 10-11, and 17-18 as not complying with the written description requirement. More specifically, the Examiner believes that the following language in the claims is not supported sufficiently by the Specification: the language referring to "variants" and "truncated variants" as well as the language referring to "a peptide which has at least about 60% sequence identity to SEQ ID NO:1, a homologue or derivative".

The test for sufficiency of support under the written description requirement of 35 U.S.C. §112, first paragraph is whether the disclosure "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." This depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure.

The Examiner states that the specification fails to disclose any substitution, insertion or deletion or change in (i) a polypeptide SEQ ID NO:1 to obtain a variant having 70% or 50% identify to SEQ ID NO:1 or variants or homologues of SEQ ID NO:1. The Examiner goes on to state that the Specification does not describe any use of such variants as claimed in identifying *L. intracellularis* infection.

First, Applicants would like the Examiner to note that the reference to truncated variants has been removed from the claims to be pursued in later filed applications. Further, Claims 1-4, 6-8, 10-11, and 17-18 all include the following functional language: "wherein said variant mimics or cross-reacts with a B-cell or T-cell epitope of Lawsonia spp. FlgE polypeptide."

The Specification provides considerable teaching of types of variants and ways of producing the variants as claimed. For example, Figure 1 provides an amino acid alignment of various FlgE polypeptides known in the art. This alignment clearly shows areas of high conservation and areas of low conservation. The amino acids that are identical in all eight sequences appear in boldface (see Brief Description of the Drawings, Figure 1). This, in combination with the specification on page 8, paragraph 98 and page 5 paragraphs 71 and 72 which explains which areas in Figure 1 are useful, the definitions of Derivatives and analogues (page 16, paragraph 194 and page 7, paragraph 89), the substitution variants (page 7 paragraphs 80-88), teachings as to the types of changes that can affect the epitope (page 6, paragraph 73), and amino acid substitutions page 4, paragraph 51, give the skilled artisan sufficient information about what types of variants would still "cross react with a B-cell or T-cell epitope of *Lawsonia spp.* FlgE Polypeptide." Once produced or identified, the variants can be tested for cross-reactivity using the methods on page 3, paragraphs 42-44.

Thus, the specification provides specific teaching on which parts of FLgE are most conserved among organisms, which areas would be most useful for antigenicity, and which areas are most unique. The specification then provides information on the types of mutations or changes which would be useful and/or accepted. The specification provides methods of testing

the variants for cross-reactivity to FlgE. Lastly, the specification provides methods of using the polypeptides as vaccines for the treatment and prophylaxis of *L. intracellularis* infection.

Because the field of vaccination and immunization is one of the earliest aspects of molecular biology to be identified, it has had a lengthy amount of time to gain a certain sophistication, while fields like immunology have lagged. Thus, the skilled artisan can be considered quite knowledgeable. Although working examples of variants and truncated variants have not been provided in the specification, the amount of guidance which has been provided gives the skilled artisan more than enough support to isolate and identify variants and truncated variants. Thus, Applicants respectfully request withdrawal of the rejection under 35 U.S.C.§112, first paragraph.

Rejection Under 35 U.S.C.§112, first paragraph (Enablement)

Claims 1-4, 6-8, 10, 11, and 17-20 were rejected because the Examiner believed that, while being enabled for an isolated polypeptide or a recombinant immunogenic polypeptide comprising the amino acid sequence of SEQ ID NO:1 or the amino acid sequence encoded by the FlgE-encoding nucleotide sequence, the specification does not necessarily provide enablement for a variant, or a truncated variant or a peptide which has at least about 60% sequence identity to SEQ ID NO:1 and a homologue or derivative.

The test for enablement involves determining whether undue experimentation is required to practice the claimed invention.

A variety of guidelines are used to identify whether undue experimentation is required to identify variants, including, the teaching in the specification, the number of known variants, and the knowledge of one of skill in the art. As stated above with respect to the written description rejection, the amount of teaching in the specification is extensive, so, although there are no working examples of variants, one of skill in the art would easily be able to make and identify variants using the teaching in the specification. In addition, the art of vaccination/immunization is one of the most sophisticated in molecular biology and, given the recent advances in the science of molecular biology, the unpredictability of this art has lessened significantly. As a result, the number of experiments necessary to determine a particular result is now low, and these experiments have become routine in the art.

Deposit

Claims 13, 14 and 23 have been rejected because they include a deposit description without a promise for availability. As suggested by the Examiner, a statement by the agent of record stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public will be irrevocably removed upon the granting of a patent is included hereinbelow, thus rendering the rejection moot.

This deposit was made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations thereunder (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit. The deposit will be made available by ATCC under the terms of the Budapest Treaty, which assures that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the pertinent U.S. patent, assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 USC § 122 and the Commissioner's rules pursuant thereto (including 37 CFR § 1.14 with particular reference to 886 OG 638). The assignee of the present application has agreed that if a culture of the cell line on deposit should die or be lost or destroyed when cultivated under suitable conditions, the materials will be promptly replaced on notification with another of the same.

Rejection Under 35 U.S.C.§102(b)

Claims 1-4, 6-8, 10, 11, and 17-18 were rejected as anticipated by McOrist et al. Infect. Immun. 1989 March; 57(3):957-962. McOrist discloses isolated protein profiles obtained with Campylobacter species and Campylobacter-like species (later identified as Lawsonia) and identifies a 55kD protein by SDS PAGE. The Examiner believes that this 55kD protein inherently anticipates the FlgE protein as claimed.

> To be anticipatory under 35 U.S.C. § 102, a reference must teach each and every element of the claimed invention. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986). "Invalidity for anticipation requires that all of the elements and limitations of the claim are found

> within a single prior art reference. ...There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565 (Fed. Cir. 1991).

The presently claimed invention is an isolated or recombinant immunogenic polypeptide, comprising a *Lawsonia* FlgE polypeptide, variant or truncated variant which mimics or cross-reacts with a B-cell or T-cell epitope of a *Lawsonia spp.* FlgE polypeptide.

McOrist et al. provides a protein profile of Campylobacter species which contains a number of different bands from 9 different preparations of various Campylobacter species. The profiles are dominated by major protein bands of 55 and 70 kD, and, as stated on page 959, column 2: "Minor components were recognized between 20,000 and 43,000 kD..." There is reference to what appears to be a 55kD band. However, with reference to the immunoblot using antiserum from rabbits injected with formalin-fixed whole cell antigen, only a 25K and 27K component was strongly recognized. The reference states that there was some recognition of the 55K and 43K bands in some preparations (see Figure 2, lane 2). However, the Examiner will note that it is very difficult to discern the presence of a band on the gel. This is particularly strange when one considers that the majority of protein identified upon SDS PAGE was the 55K and 43K band. When transferring from an SDS gel to a western blot, the strongest band (having the most protein) will transfer as the band having the most protein on the blot. However, because this band is very weak to nonexistent on the Western, it is likely that the 55K band was either very weakly antigenic or not antigenic at all. The staining on the Western could easily have been a false positive due to over-loading of the gel.

The Examiner states that "it is inherent that the 55 kD antigen isolated/identified by polyacrylamide gel electrophoresis procedure is the same as the claimed polypeptide." However, according to the MPEP §2112 IV. "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill". The Examiner must provide rationale or evidence tending to show inherency. "The Fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish inherency..."

The Examiner's identification of a possible band on an SDS PAGE gel at approximately 55 kD does not constitute evidence to show inherency. Due to the inexact nature of SDS PAGE gels, this band could have had a molecular weight varying between 50 and 60kD. Further, as

mentioned previously, the band that the Examiner identifies was found to be very weakly identified in one of 5 preparations by immune serum from an animal, suggesting to the skilled artisan that it was weakly immunogenic or not antigenic at all. The skilled artisan is aware that when there is an abundance of protein in a gel, it is much more likely to show a false positive on an immunoblot. Thus, that fact that the putative 55 kD band was shown upon further analysis by immunoblot to be weakly immunogenic, and the polypeptide recited in the presently pending claims are claimed as immunogenic, whatever the "55 kD antigen" isolated by McOrist is, it is unlikely to represent the polypeptide recited in the presently pending claims.

Thus, Applicants submit that the putative 55 kD band is not inherently the same as an isolated immunogenic FlgE polypeptide as claimed herein and Applicants respectfully request withdrawal of the novelty rejection.

Rejection Under 35 U.S.C.§102(b)

Claims 1-4, 6-8, 10, 11, and 17-18 were rejected as anticipated by Panaccio, et al. 1997, Database: A Geneseq and Accession number AAW16680, WO9720050-A1. Panaccio disclose an isolated or recombinant polypeptide (SEQ ID NO:7 page 51-52 and claim 26) comprising a 120 amino acid Lawsonia intracellularis FlgE polypeptide variant or having 100% identity to SEQ ID NO:1 (from position 64 to 84).

However, the claims have been amended to remove the reference to truncated variants to be pursued in separate applications. Panaccio, et al. specifically teaches a truncated variant which could potentially be used for protection of animals to L. intracellularis. Panaccio et al. does not teach or suggest the variants of SEQ ID NO:1 or a variant with 60% sequence identity to the full sequence of SEQ ID NO:1, because Panaccio et al. does not teach the rest of the polypeptide.

Applicants respectfully request withdrawal of the novelty rejection.

Conclusion

Applicants believe that the current amendments place the application in condition for allowance. Should there be any questions which might result in a delay in allowance, the examiner is respectfully requested to contact the undersigned at the telephone number appearing below. Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: May 16, 2005

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